

REVIEW

Amiodarone and the thyroid: a practical guide to the management of thyroid dysfunction induced by amiodarone therapy

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Amiodarone is a highly effective agent for the prophylaxis and treatment of many cardiac rhythm disturbances, ranging from paroxysmal atrial fibrillation to life threatening ventricular tachyarrhythmias.¹ Unlike many other anti-arrhythmic drugs, amiodarone appears to be safe in patients with significant left ventricular dysfunction,²⁻⁵ and may confer prognostic benefit in some patient subgroups.^{6,7}

Amiodarone bears a remarkable structural resemblance to thyroid hormones. The free base contains 39% iodine by weight (fig 1), and chronic treatment is associated with 40-fold increases in plasma and urinary iodide levels.⁸ Amiodarone has complex effects on thyroid physiology in all patients taking the drug, and chronic treatment is associated with substantial changes in the results of standard thyroid function tests. Although most patients remain clinically euthyroid, a significant minority (up to 15% of patients in the UK and the USA) develop amiodarone induced hypothyroidism or thyrotoxicosis.⁹⁻¹² Unfortunately, amiodarone induced thyroid dysfunction is rarely man-

ageable by discontinuation of amiodarone alone, partly because it has an extremely long terminal half life (up to four months).¹³ The purposes of this review are to summarise expected and abnormal changes in thyroid function in patients taking amiodarone, and to suggest guidelines for the diagnosis and management of amiodarone induced thyroid dysfunction.

Normal thyroid physiology: effects of amiodarone in euthyroid patients

The synthetic pathways of thyroxine (T₄) and triiodothyronine (T₃), along with the sites of action of antithyroid drugs, are summarised in fig 2. The expected effects of amiodarone treatment on individual biochemical parameters of thyroid function are outlined below and summarised in table 1, along with a simplified and practical account of the underlying mechanisms. A more comprehensive discussion has been published.¹⁴ The reference ranges quoted are those used at our own institution; some variation will clearly exist between laboratories, which should be taken into account when interpreting the results of thyroid function tests in individual patients.

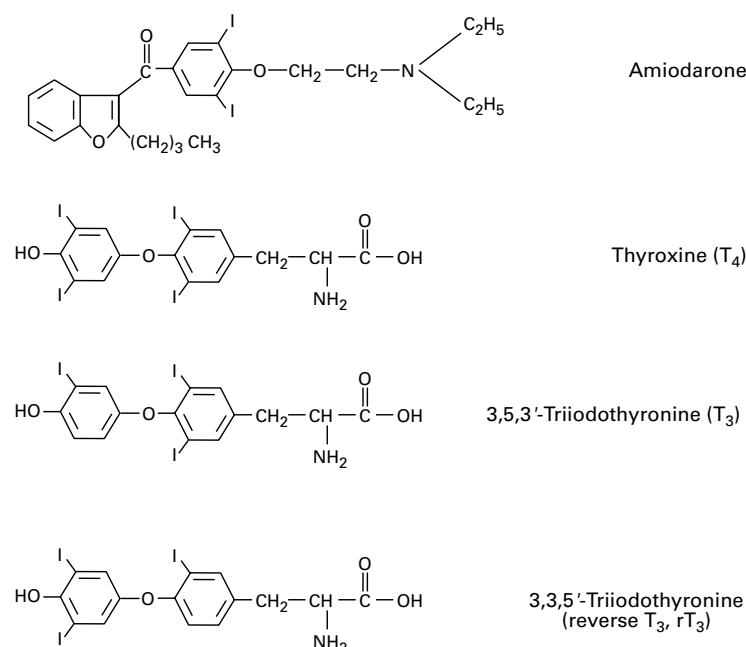


Figure 1 Structure of amiodarone and thyroid hormones.

SERUM T₄ AND T₃

The pharmacological consequences of iodide associated with amiodarone treatment lead acutely to a protective inhibition of thyroidal T₄ and T₃ production and release (the Wolff-Chaikoff effect) within the first two weeks of treatment.¹⁵ The thyroid eventually escapes from this effect, which restores T₄ production to normal or even raised concentrations despite continued amiodarone administration. Amiodarone also inhibits the 5' deiodination of T₄ to T₃ in the peripheral tissues, especially the liver. This inhibitory action persists during, and for several months after, amiodarone treatment. The net result is that serum T₄ rises from pre-treatment concentrations by an average of 40% after two months and remains at this higher level thereafter.^{10,16,17} The absolute serum T₄ concentrations in patients on moderate doses of amiodarone (200 mg/day) is usually towards the upper limit of the reference range (71-166 nmol/l). A minority of clinically euthyroid patients, however, will have serum T₄

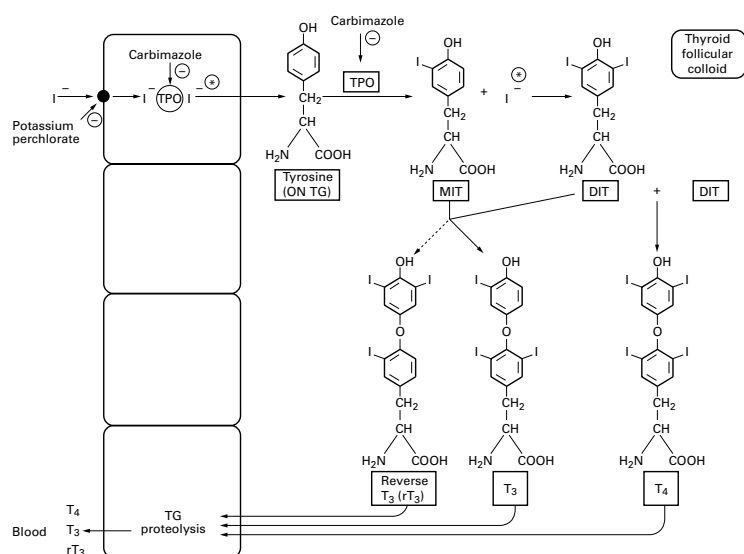


Figure 2 Synthetic pathway of thyroid hormones. The organification of oxidised iodine takes place at the apical membrane of the thyrocyte and involves iodination of tyrosine residues on thyroglobulin (TG) molecules stored in the thyroid follicular colloid. Monoiodotyrosine (MIT) residues and diiodotyrosine (DIT) residues within the same and adjacent thyroglobulin molecules then combine to form triiodothyronine (T_3 , the major biologically active hormone), thyroxine (T_4), and, to a limited extent, the inactive compound reverse triiodothyronine (rT_3). Thyroid hormones are cleaved from thyroglobulin after pinocytosis of colloid into the thyrocyte, and are then released into the circulation. The thyroid gland is the only source of circulating T_4 , whereas 80% of circulating T_3 is generated by deiodination of T_4 in peripheral tissues, especially the liver. The sites of action of antithyroid drugs are highlighted. TPO, thyroid peroxidase; I^* , oxidised form of iodide.

concentrations greater than 166 nmol/L, and this increases with higher daily doses of amiodarone.¹⁰

Serum T_3 concentrations fall during amiodarone treatment, initially in part due to reduced thyroid synthesis, but principally because of reduced 5' deiodination of T_4 to T_3 in peripheral tissues.^{18–20} T_3 concentrations usually remain within the reference range (1.3–3.0 nmol/l), but occasionally fall below 1.3 nmol/l.

FREE T_4 (FT_4) AND FREE T_3 (FT_3)

As amiodarone has no effect on the serum concentration of thyroid hormone binding globulin,¹⁶ changes in FT_4 and FT_3 concentrations mirror those for total T_4 and T_3 .

SERUM REVERSE T_3 (rT_3)

Reduced peripheral metabolism leads to increased rT_3 concentrations with amiodarone treatment, but the assay is not widely employed, largely because rT_3 is biologically inactive.

SERUM THYROID STIMULATING HORMONE (TSH)

Serum TSH rises transiently within a few days of starting amiodarone, but rarely reaches

Table 2 Reference ranges for thyroid hormone concentrations in euthyroid untreated patients and in clinically euthyroid patients on long term amiodarone treatment

Test	Untreated patients	Patients on chronic amiodarone treatment
TSH (mU/l)	0.35–4.3	—
FT_4 (pmol/l)	11–20	12–24.7 (382)*
FT_3 (pmol/l)	3–5.6	2.5–5.1 (189)
T_4 (nmol/l)	71–166	—
T_3 (nmol/l)	1.3–3.0	1.0–2.3 (169)

The reference ranges for thyroid hormone concentrations during chronic amiodarone treatment were constructed from patients with TSH within the reference range for clinically euthyroid untreated patients.

*Sample size used to generate each reference range.

greater than 20 mU/l (reference range 0.35–4.3 mU/l).^{17–21} TSH then gradually return to baseline concentrations, or even slightly below, over the next one to three months.^{17–21–22}

The early rise in plasma TSH occurs largely in response to falling intrapituitary T_3 concentrations consequent on reduced 5' deiodination of T_4 to T_3 , especially within the pituitary. Furthermore, desethylamiodarone (DEA), the principal metabolite of amiodarone, binds to intracellular T_3 receptors and acts as a T_3 antagonist.²³ TSH falls over the next few weeks as total T_4 concentrations rise sufficiently to overcome the partial block in T_3 production.

Suppression of TSH to low or even undetectable levels (< 0.03–0.35 mU/l) can occur for short periods in clinically euthyroid patients during the course of amiodarone treatment, possibly reflecting subclinical episodes of amiodarone induced destructive thyroiditis and thyrotoxicosis. Conversely, some clinically euthyroid patients experience periods of modestly raised TSH (> 4.3–20 mU/l) during chronic treatment, which could reflect episodes of subclinical hypothyroidism. To complicate matters further, non-thyroidal illnesses can have profound effects on the results of standard thyroid function tests, including TSH.²⁴ A single abnormal TSH is therefore insufficient to make a confident diagnosis of either thyrotoxicosis or hypothyroidism and additional information is required.

An alternative method for describing these expected effects of amiodarone on thyroid function tests is to construct new reference or normal ranges for patients on long term amiodarone treatment. Table 2 compares our reference ranges for thyroid function tests in untreated and amiodarone treated individuals, the latter based on an audit of 382 patients who were clinically euthyroid and in whom serum TSH was within the euthyroid reference range for untreated individuals. There will clearly be some variation in reference ranges between laboratories, but the percentage shifts between the ranges for untreated and treated patients should be similar.

In summary, chronic amiodarone treatment (more than three months) in clinically euthyroid patients is usually associated with high-normal or raised T_4 and FT_4 , low-normal T_3 and FT_3 , low-normal TSH, and high rT_3 concentrations.

Table 1 Effects of amiodarone on thyroid function tests in euthyroid patients

Test	Duration of treatment	
	Subacute (up to 3 months)	Chronic (> 3 months)
T_4	Modest increase	Remains increased by up to 40% above baseline; may be in high reference range or modestly raised
T_3	Decreased, usually to low reference range	Remains in low reference range or slightly low
TSH	Transient increase (up to 20 mU/l)	Normal, but may be periods of high or low values
rT_3	Increased	Increased

Amiodarone induced hypothyroidism

The reported incidence of amiodarone induced hypothyroidism (hereafter abbreviated to hypothyroidism) varies widely, ranging from as high as 13% in countries with a high dietary iodine intake (such as the UK and USA)^{9 10 12} to as low as 6% in countries with low or intermediate iodine intake (such as Italy and Spain).^{9 22} The risk of developing hypothyroidism is independent of the daily or cumulative dose of amiodarone, but is enhanced in elderly and female patients.^{9 14 16 27} This is to be expected as autoimmune thyroid disease is the principal risk factor for the development of hypothyroidism and is particularly common in these patient groups. Indeed, the combination of female sex and the presence of thyroid peroxidase or thyroglobulin antibodies constitutes a relative risk of 13.5 for the development of hypothyroidism.²⁷

The most likely explanation for the development of hypothyroidism is an inability of the thyroid to escape from the acute inhibitory effects of iodine on hormone release and synthesis. As mentioned above, this may reflect underlying thyroid disease, as hypothyroidism is also a well recognised outcome in patients with subclinical autoimmune thyroiditis given excess iodine and generally occurs relatively early (three to 12 months) after starting treatment with amiodarone.^{14 28} It is also possible that excess iodine may exacerbate pre-existing autoimmune thyroiditis directly in some patients, particularly those from areas of low dietary iodine intake.^{29 30}

The diagnosis of hypothyroidism is usually straightforward. The clinical features are not affected by amiodarone, although most patients have very few symptoms, most commonly increased lethargy. The diagnosis is confirmed by finding a raised TSH concentration, usually above 20 mU/l, in combination with low T₄ or FT₄.³¹ Low T₃ or FT₃ concentrations are an unreliable indicator of hypothyroidism as they may occur in euthyroid patients during amiodarone treatment. A goitre is found in about 20% of patients with hypothyroidism in iodine replete areas, but most of these goitres predate the start of amiodarone treatment.¹⁴

The purist's approach to the treatment of hypothyroidism is to stop amiodarone. As many physicians only use amiodarone in high risk patients or when other agents have failed to control symptoms, this is rarely an acceptable option. Many patients without pre-existing thyroid disease will become euthyroid within two to four months of stopping amiodarone, but permanent hypothyroidism requiring T₄ replacement is common in patients with thyroid antibodies.³² Restoration of euthyroidism once amiodarone is stopped can be accelerated by the administration of potassium perchlorate in a single daily dose of 1.0 g for up to five weeks.^{33 34} This agent competitively inhibits thyroid iodide uptake, which leads to passive discharge of iodide from the thyroid; the consequent fall in intrathyroidal concentration diminishes the inhibitory effects of iodide on hormone synthesis. Unfortunately, hypo-

thyroidism recurs in 50% of cases within a few weeks of stopping treatment, and there is a significant risk of aplastic anaemia, nephrotic syndrome, gastrointestinal upset or rash occurring, so this treatment cannot generally be recommended.

By far the safest, quickest, and most reliable treatment for hypothyroidism is to continue amiodarone and to add T₄, increasing the dose at monthly intervals until the TSH concentration is well within the normal range and symptoms attributable to hypothyroidism have resolved. Although this is generally easy to administer, a recent consensus statement suggested that all patients with hypothyroidism should be referred to an endocrinologist in the first instance.³⁵ This may be especially worthwhile in elderly patients and if there are particular complications from the underlying cardiac disorder.

A pattern of moderately raised TSH (> 4.3–20 mU/l), but high-normal or raised T₄ and/or FT₄ concentrations indicates early or subclinical hypothyroidism.³⁶ If thyroid antibodies are present, treatment with T₄ should be instituted without further delay, as such patients are very likely to progress to overt hypothyroidism. Those without antibodies but with symptoms potentially attributable to hypothyroidism should be given a three month trial of T₄ and then reassessed for symptomatic improvement.³⁶ In the absence of symptoms or antibodies, continued follow up at frequent intervals (ideally at six weeks, then every three months) is required, as some patients will progress to overt hypothyroidism.³⁶ It is particularly important to remember that FT₄ concentrations in the middle of the reference range are inappropriate for an amiodarone treated patient and, in combination with raised TSH, may well represent hypothyroidism requiring treatment. The advice of an endocrinologist may be useful in patients with subclinical hypothyroidism taking amiodarone.

Amiodarone induced thyrotoxicosis

Though much less common than hypothyroidism in iodine replete areas such as the UK and USA (< 2% v 13%),^{9 10 12} the pathogenesis of amiodarone induced thyrotoxicosis (hereafter abbreviated to thyrotoxicosis) is more complex and the diagnosis and treatment much more difficult; an endocrinologist's opinion is definitely recommended in all such cases.³⁵ Thyrotoxicosis occurs more frequently in men and in iodine deficient areas, but there is no relation between the daily or cumulative dose of amiodarone and the incidence of thyrotoxicosis.^{9 11 14 37} The onset of thyrotoxicosis is often acute and may occur several months after the discontinuation of treatment.²⁷ Spontaneous remissions are common.

The clinical features of thyrotoxicosis are sometimes obscured by the antiadrenergic effects of amiodarone, but new or recurrent atrial arrhythmias during chronic treatment should arouse the suspicion of thyrotoxicosis. The biochemical diagnosis is straightforward if T₃ or FT₃ concentrations are raised and TSH is suppressed to undetectable concentrations,

Table 3 Pathogenesis and clinical features of amiodarone induced thyrotoxicosis

	Type I	Type II
Underlying thyroid abnormality	Yes	No
Pathogenetic mechanism	Excessive hormone synthesis due to iodine excess	Excessive release of preformed hormones due to thyroid destruction
Goitre	Multinodular or diffuse goitre normally present	Occasionally small, diffuse, firm, sometimes tender
Thyroidal radioiodine uptake	Normal/raised	Low/absent
Serum IL-6	Normal/slightly raised	Profoundly raised
Thyroid ultrasound	Nodular, hypoechoic, increased volume	Normal

particularly as T_3 is never raised in euthyroid patients during amiodarone treatment. In some cases, however, TSH may be undetectable (< 0.03 mU/l) or significantly suppressed (≥ 0.03 – 0.35 mU/l), along with high-normal or raised T_4 and FT_4 concentrations, but T_3 and FT_3 concentrations remain at the lower end of the reference range. This pattern may represent early or subclinical thyrotoxicosis; this diagnosis is made more likely if raised serum sex hormone binding globulin and/or ferritin are also present, as both of these are useful if rather non-specific markers of tissue thyroid hormone excess. The same pattern of thyroid function test results can, however, be seen in clinically euthyroid patients with non-thyroidal illnesses, when it is termed the sick euthyroid syndrome.²⁴ To distinguish between these possibilities, further thyroid function tests should be performed six weeks later. If the patient is well (or has recovered from such an illness) and yet TSH remains suppressed, then a diagnosis of thyrotoxicosis can be made with confidence.

There are two main forms of thyrotoxicosis (table 3) that have differing aetiologies and require different treatment.^{14 38 39} Type I thyrotoxicosis occurs in patients with underlying thyroid pathology, such as latent Graves' disease or nodular goitre. In these patients, the sudden iodide load associated with amiodarone treatment accelerates thyroid hormone synthesis sufficiently to induce thyrotoxicosis, owing to increased thyroid hormone production in subclinically autonomous thyroid tissue. This iodide induced thyrotoxicosis, an example of the Jod-Basedow phenomenon, is identical to that seen in patients with endemic iodine deficient goitre who are then given iodide replacement, thus explaining why thyrotoxicosis is more common in iodine depleted areas. In contrast, type II thyrotoxicosis occurs in an apparently normal thyroid, and results from a direct toxic effect of amiodarone causing a subacute destructive thyroiditis with consequent leakage of preformed thyroid hormones into the circulation.

Distinguishing between thyrotoxicosis types I and II is important as it has a major influence on subsequent management (table 3). Clinical evidence of a multinodular goitre or, rarely, Graves' ophthalmopathy is only found in type I thyrotoxicosis. A small, often tender, goitre may be found in type II thyrotoxicosis. The most useful discriminator, however, is the radioactive iodine uptake (RAIU) test. RAIU is normal or raised in type I thyrotoxicosis

because of avid uptake by autonomous thyroid tissue, but is very low or absent in type II thyrotoxicosis due to destruction of or damage to thyroid tissue. Thyrotoxicosis types I and II are further differentiated by measurements of inflammatory mediators, particularly interleukin 6 (IL-6), which is profoundly increased in thyrotoxicosis type II but is normal or modestly raised in type I.^{38 39} Finally, thyroid ultrasonography often reveals an increased thyroid volume, a hypoechoic pattern, and nodular lesions in thyrotoxicosis type I but is normal in type II.^{39 40}

In practice, the diagnosis of thyrotoxicosis type I or II is not always clear cut. Some patients exhibit a mixed picture, combining features of pre-existing thyroid disease (for example, a multinodular goitre) with evidence of a superimposed amiodarone induced thyroiditis (for example, an explosive onset and a subnormal RAIU).

There has been no large controlled trial to determine the optimal management of thyrotoxicosis, and indeed treatment strategies may vary between regions depending on dietary iodine intake. From an endocrinological viewpoint, the management of thyrotoxicosis is facilitated by the withdrawal of amiodarone. This reduces iodide stimulated thyroid hormone production in thyrotoxicosis type I and removes the stimulus to amiodarone induced thyroiditis in thyrotoxicosis type II. In many cases, however, this is an unattractive option to the referring physician, and considerations such as the clinical condition of the patient, the original indication for amiodarone, and the availability of effective alternatives also influence this decision. The final management plan for each patient must be decided on jointly, and the following are simply general guidelines.

MANAGEMENT OF THYROTOXICOSIS WHEN AMIODARONE CAN BE STOPPED

If the original indication for amiodarone was a non-life threatening arrhythmia such as paroxysmal atrial fibrillation, then replacing amiodarone with an alternative form of treatment may be a reasonable option. It should be remembered, however, that amiodarone and its metabolites have actions that may, paradoxically, serve to protect the patient from some of the effects of thyrotoxicosis. In particular, amiodarone has β adrenoreceptor blocking activity, and DEA is a potent T_3 receptor antagonist. Worsening of thyrotoxic symptoms and cardiac status have indeed been reported following withdrawal of amiodarone.^{41 42}

Patients with thyrotoxicosis type I rarely respond to withdrawal of amiodarone alone; most are still hyperthyroid six to nine months after discontinuation of the drug.³² The management of thyrotoxicosis type I in these patients therefore centres upon the use of thiourea derivatives, particularly carbimazole, to block hormone synthesis while amiodarone and its associated iodine are cleared from the body.^{11 37 39} The massively raised thyroidal iodide concentrations found in patients on amiodarone reduces the effectiveness of carbimazole because the mechanism of action

involves iodination of the drug, which in turn reduces the availability of free iodide for hormone synthesis. High doses of carbimazole, 40–60 mg daily in divided doses, are therefore required. Propylthiouracil (100–150 mg four times a day) can also be used and has the theoretical advantage that it also inhibits peripheral 5' deiodinase activity.^{43 44} If necessary, potassium perchlorate (0.5 g twice a day) can also be given to block iodide uptake, which, in turn, reduces intrathyroidal iodide treatment enhancing the efficacy of carbimazole. Antithyroid drugs may be continued for three to six months, and a minority of patients with underlying Graves' disease will remain permanently euthyroid once treatment (including amiodarone) is discontinued. All these antithyroid drugs can cause bone marrow suppression and patients must be advised of warning signs such as fever, sore throat or oral ulceration.

As most patients with thyrotoxicosis type I will have underlying Graves' disease or toxic multinodular goitre, thyrotoxicosis usually recurs and definitive treatment, usually radioiodine, is therefore recommended. The timing of this depends on the severity of thyrotoxicosis, the response to antithyroid drugs, the RAIU level, and the policy of the supervising endocrinologist.

Withdrawal of amiodarone may suffice in patients with thyrotoxicosis type II, no symptoms of thyrotoxicosis, and no worsening of their cardiac condition. The majority of such patients will become and remain euthyroid within three to five months of amiodarone withdrawal.³² Steroid treatment accelerates recovery and should be used in all patients with symptoms of thyrotoxicosis and/or worsening of their underlying arrhythmia. Prednisolone 40–60 mg daily is used, tailed off gradually over three months depending on response, with careful follow up as the disease may recur.^{11 37 39} In most cases, biochemical and clinical resolution of thyrotoxicosis begins within days of commencing steroids and is complete within the first month of treatment.³⁹

Free thyroidal iodide is a tiny fraction of total thyroid iodine; the majority is contained in preformed thyroid hormones and their precursors. Continued iodide uptake therefore depends on depletion of thyroidal free iodide by active organification. It is not surprising, therefore, that treatment with antithyroid drugs alone is often unsuccessful in type II thyrotoxicosis, as the low RAIU in this condition indicates a very low concentration of ongoing iodide organification.^{32 44 45} Indeed, a recent study showed that steroid treatment alone is sufficient in pure thyrotoxicosis type II,³⁹ although previous studies have combined steroids with antithyroid drugs.⁴⁵ Radioiodine treatment is not effective in thyrotoxicosis type II. Alternative treatment for the underlying arrhythmia should be instituted if symptoms recur.

Mixed forms of thyrotoxicosis are usually treated with a combination of both antithyroid drugs and prednisolone, at least in the first instance, as are patients in whom the full range of diagnostic tests to differentiate thyrotoxico-

sis types I and II are not available or if the results are inconclusive.

MANAGEMENT OF THYROTOXICOSIS WHEN AMIODARONE CANNOT BE STOPPED

Although there are no good data to confirm or quantify the perceived risks, discontinuation of amiodarone in patients with thyrotoxicosis and a history of serious, especially ventricular, arrhythmias is theoretically hazardous for several reasons. First, cessation of amiodarone may exacerbate the thyrotoxic/cardiac status of the patient.^{41 42} Second, alternative treatment strategies, such as ablation or implantable defibrillators, may not be appropriate and not all patients will have undergone a detailed assessment for such treatments before amiodarone therapy. Furthermore, a *de novo* assessment may be difficult, perhaps impossible, to interpret in a thyrotoxic patient recently treated with amiodarone. Third, alternative drugs may well have been tried unsuccessfully before the institution of amiodarone. Finally, the consequences of beginning treatment with any new antiarrhythmic drug in a thyrotoxic patient whose tissues, including the myocardium, are still saturated with amiodarone cannot be predicted with any certainty. In general, therefore, it is safer to persist with amiodarone and treat the thyrotoxicosis as aggressively as the clinical situation demands.

Continuation of amiodarone does not alter the basic approach to the medical management of thyrotoxicosis but reduces the chances of a successful outcome. In thyrotoxicosis type I, the effectiveness of antithyroid drugs and radioiodine is reduced by the persistently raised thyroidal and circulating iodide levels. Spontaneous remission of thyrotoxicosis type II (but not type I) can occur despite continued treatment,¹⁴ however, and there are reports that treatment with antithyroid drugs, maintained until TSH concentrations recover, can be associated with a permanent cure.^{44 45}

Subtotal or, ideally, near total thyroidectomy is a definitive and often preferred treatment for both forms of thyrotoxicosis when withdrawal of amiodarone is not an option.^{42 46 47} Thyroidectomy is also indicated when immediate control of the thyrotoxic state is required, as during thyroid storm or severe cardiac failure, and in those with intractable arrhythmias. Even in such ill patients, surgery is associated with a surprisingly low morbidity and mortality.^{42 46 47} The operation has even been performed successfully after local anaesthesia in a patient judged to be too ill for general anaesthesia.⁴⁸ Plasmapheresis has been used in severe thyrotoxicosis,^{49 50} not always successfully,⁵¹ and surgery seems, on balance, to offer a better outcome in acutely ill patients.

Monitoring thyroid function in patients taking amiodarone

Baseline thyroid function testing should be undertaken before starting treatment and should include serum TSH and thyroid antibodies as a minimum (fig 3). Patients with pretreatment TSH concentrations towards the upper end of the reference range and/or thyroid

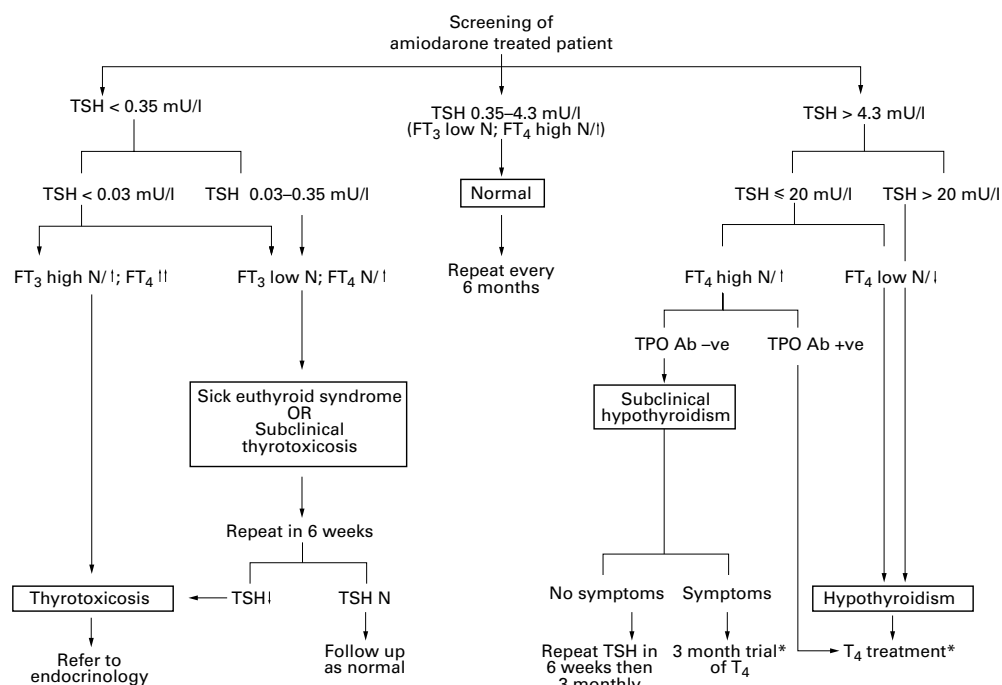


Figure 3 Suggested protocol for screening thyroid function in patients treated with amiodarone. TPO, thyroid peroxidase; * amiodarone withdrawal considered an alternative option in some cases.

antibodies are at increased risk of developing hypothyroidism and require close follow up: those with subnormal TSH concentrations are probably at increased risk of developing thyrotoxicosis type I. TSH concentrations should be measured every six months during treatment, primarily to permit the identification of insidious hypothyroidism. If equivocal biochemical results are obtained in clinically euthyroid patients, suggestive of subclinical hypothyroidism or thyrotoxicosis, then further testing in six weeks is recommended. The presence of thyroid antibodies in patients with a moderately raised TSH is strong supportive evidence of hypothyroidism and probably merits treatment with T_4 without further delay.

Thyrotoxicosis type II has an explosive onset, and is difficult to predict. It may develop at any time during treatment, often accelerating in severity over only a few days. There should therefore be a low threshold for performing thyroid function tests in any suspicious circumstances when a patient is taking amiodarone. As thyrotoxicosis type I can occur months or even years after discontinuation of amiodarone, there should also be a low threshold for thyroid function testing if amiodarone has been discontinued for reasons other than thyroid dysfunction. Some patients with treated thyrotoxicosis type II will eventually become hypothyroid due to extensive damage to thyroid tissue, as will some type I patients treated with radioiodine. Careful and prolonged monitoring of thyroid function in all patients with a history of thyrotoxicosis is therefore mandatory, even after amiodarone is withdrawn.

Summary

Amiodarone induces predictable changes in thyroid function tests that are largely explicable

in terms of the physiological effects of iodide excess and inhibition of deiodinase activity. Clinically relevant thyroid dysfunction is not uncommon during amiodarone therapy, and requires careful diagnosis and treatment. The diagnosis and management of thyrotoxicosis is probably best supervised by a specialist endocrinologist. Control of hypothyroidism can generally be achieved simply by the addition of T_4 to the therapeutic regimen, ideally after an initial assessment by an endocrinologist. The frequency with which amiodarone causes thyroid and other complications serves to emphasise the need for rational prescribing and long term cardiological follow up.

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